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TOXICOLOGICAL EVALUATION OF CARBORANYLMETHYL PROPIONATE.(U)
JUL 77 J A MACKO, J G HARVEY, C R POPE

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TOXICOLOGICAL EVALUATION OF CARBORANYLMETHYL PROPIONATE

STUDY NO. 51-0845-77

DECEMBER 1975 - SEPTEMBER 1976

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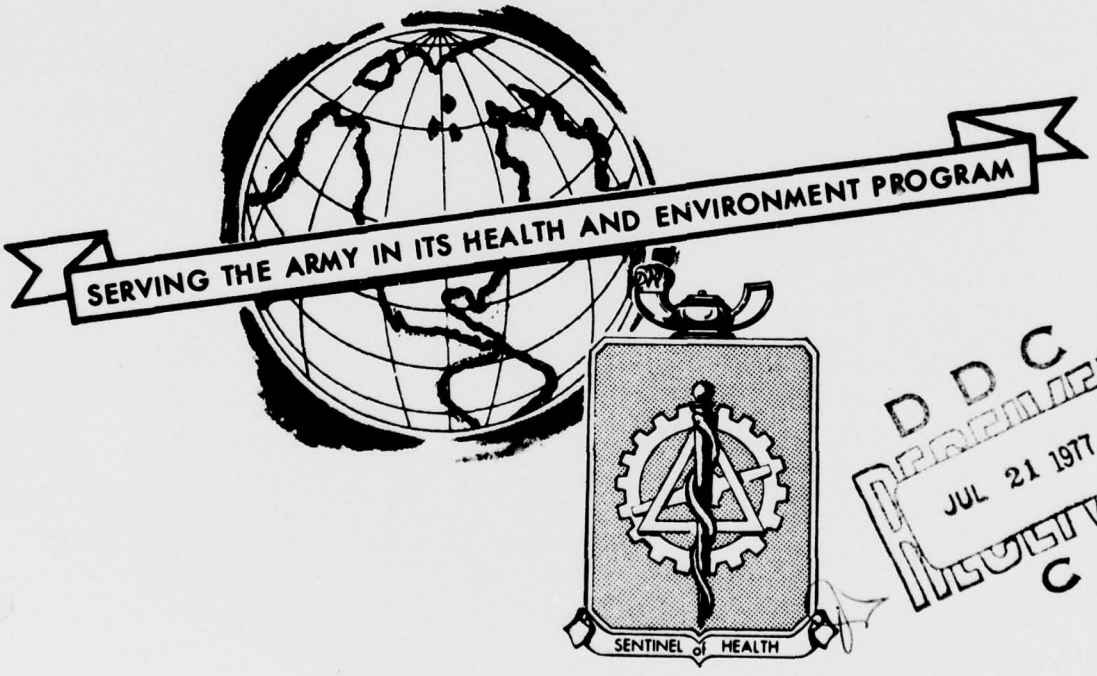

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

toxicological evaluation	Approximate Lethal Dose	In Vitro Mutagenic
carboranylmethyl propionate	Acute Inhalation Vapor Exposure	Evaluation
skin irritation	Acute Inhalation Aerosol Exposure	
photochemical skin irritation	Subchronic Inhalation	Enzyme Induction
sensitization studies	Prenatal Toxicity	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The relative toxicity of technical grade carboranylmethyl propionate was investigated using rats, guinea pigs and rabbits. Compound produced acute primary skin irritation and was classified only slightly toxic when applied dermally. Classified moderately toxic by ingestion with no deleterious effects found after acute and subchronic saturated vapor inhalation exposure. It was recommended that personnel potentially exposed to carboranylmethyl propionate wear protective gloves, coveralls and goggles. Medical surveillance of workers involved in handling this material should take cognizance of the potential for irritation of the respiratory tract, skin and eyes.

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DEPARTMENT OF THE ARMY
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12 JUL 1977

HSE-LT/WP

TOXICOLOGICAL EVALUATION OF CARBORANYLMETHYL PROPIONATE STUDY NO. 51-0845-77 DECEMBER 1975 - SEPTEMBER 1976

ABSTRACT

The relative toxicity of technical grade carboranylmethyl propionate was investigated using rats, guinea pigs and rabbits. The compound produced primary irritation when applied to the intact and abraded skin of rabbits. Dilutions of carboranylmethyl propionate with hexane were found to be more irritating to intact skin than equivalent dilutions of carboranylmethyl propionate with acetone. Data indicate moderate toxic hazard would be expected from acute accidential ingestion. Test compound is classified slightly toxic when applied dermally. Acute and subchronic saturated vapor inhalation exposures of animals resulted experimentally in no deleterious effect from the test compound. Acute aerosol inhalation exposures of rats caused some respiratory irritation and corneal damage. Carboranylmethyl propionate does not appear to present any significant hazard to subsequent generations based on teratology studies and the results of mutagen testing on standard strains of bacteria and yeast. Carboranylmethyl propionate was also found not to induce hepatic microsomal enzyme activity.

It was recommended that personnel potentially exposed to carboranylmethyl propionate wear protective gloves, coveralls and goggles. Medical surveillance of workers involved in handling this material should take cognizance of the potential for irritation of the respiratory tract, skin and eyes.

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HSE-LT/WP

TOXICOLOGICAL EVALUATION OF
CARBORANYLMETHYL PROPIONATE
STUDY NO. 51-0845-77
DECEMBER 1975 - SEPTEMBER 1976

1. AUTHORITY. Letter, BMDATC-MT, Ballistic Missile Defense Advanced Technology Center, 3 December 1975, subject: Toxicological Evaluation of Several Carboranyl Compounds, and indorsement thereto.

2. REFERENCES.

a. Report, this Agency, Toxicological Evaluation of n-Hexyl Carborane, Carboranylmethylethyl Sulfide and Carboranylmethylpropyl Sulfide, Study No. 51-044-74/76, January 1974 - May 1975.

b. Letter, BMDATC-M, Ballistic Missile Defense Advanced Technology Center, 21 January 1976, subject: Evaluation of Mutagenic Characteristics of Carboranylmethyl Propionate.

c. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency Agency (USAEHA), 1972.

3. PURPOSE. The purpose of this study was to acquire information concerning the toxicity in animals of carboranylmethyl propionate (propanoate) (CMP). This information provides a basis for advising on possible hazards associated with the manufacture of this compound and safety precautions to be observed in its handling (reference para 1a).

4. BACKGROUND.

a. The US Army Environmental Hygiene Agency has performed toxicological evaluations of several carboranyl compounds, n-hexyl carborane (NHC), carboranylmethylethyl sulfide (CMES) and carboranylmethylpropyl sulfide (CMPS), which are of critical interest to the US Army Missile Command because they are ingredients of the ultrahigh burning rate propellents which are under development (reference para 2a). CMP is an additional carborane of interest because it is a constituent of the ultrahigh burning rate composite-modified double-base propellants. Knowledge of the toxicological properties of CMP are needed to base industrial hygiene and engineering procedures in order to control any potential hazards associated with its manufacture and processing into solid fuel.

b. A literature search using the data base of the National Library of Medicine revealed no mammalian toxicological data pertaining to CMP.

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c. CMP (lot number 103057) was obtained through the Ballistic Missile Defense Advanced Technology Center, Alabama, from the manufacturer, Hercules Incorporated, Cumberland, Maryland. An additional quantity of CMP was obtained from Rockwell International Corporation, Conoga Park, California. CMP is a colorless liquid with a density of 1.05 g/ml, a boiling point of 125°C/1mm, a melting point of 20°C and a refractive index of 1.564 (n_D) (25°C) (reference para 2b). The compound is soluble in organic solvents, such as hexane and acetone, but not soluble in water.

5. SUMMARY OF FINDINGS. The relative toxicity of technical grade CMP was investigated by this Agency using Sprague-Dawley, Wistar derived rats, New Zealand White rabbits and Hartley guinea pigs. This compound was found to be a primary skin irritant in the technical grade form. Dilutions of CMP with hexane were found to be more irritating after 24 hours than an equivalent dilution of the test compound with acetone. The diluent hexane alonewas found to be slightly irritating to the skin of rabbits after 24 hours but the diluent acetone caused no irritation over the same time period. Data indicated that CMP administered orally to rats was moderately toxic. The intravenous approximate lethal dose (ALD) in male rabbits was 192 mg/kg and the intraperitoneal ALD in male rats was 851 mg/kg. CMP is classified as only slightly toxic when administered dermally to rabbits. This carborane did not cause skin sensitization reactions in guinea pigs, nor photochemical skin irritation in rabbits. However, an ethanol solution of CMP caused the same degree of erythema and edema at both irradiated and nonirradiated skin sites. No prenatal toxicity was observed when CMP was administered orally to pregnant albino rats. Single 8 hour saturated vapor exposures generated at 24°C and 100°C and daily 6 hour exposures for 2 weeks at the same temperatures resulted experimentally in no deleterious effects. Acute 1 hour aerosol exposures to 2.5 mg/l nominal and 4.7 mg/l nominal caused some lung irritation in rats. Corneal damage was observed in rats exposed to the higher aerosol concentration. In vitro mutagenic studies in microbial assays indicated that CMP was not mutagenic to bacterial or yeast test systems. CMP does not appear to present any significant hazard to subsequent generations based on teratology studies. CMP was also found not to induce hepatic microsomal enzyme activity following intraperitoneal injections. Definitions of selected terms and abbreviations used in this report are found in Appendix A. Statistical significance in this report has been selected at the 0.01 level of probability. Infrared spectra of the technical grade compound is found in Appendix B. A detailed tabular presentation of toxicity data developed in this Agency follows:*

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* The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," as prepared by the Committee on Revision of the "Guide for Laboratory Animal Facilities and Care," of the Institute of Laboratory Animals Resources, National Research Council (1972), and were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Annimal Care.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Skin Irritation Study		
Rabbits		
Primary Irritation Evaluation		
Single 24-hour applications of CMP to intact and abraded skin of New Zealand White rabbits.	Slight to well defined erythema and no irritation to well defined edema of intact and abraded skin were present 24 hours after application. Well defined to moderate erythema and no irritation to slight edema of intact and abraded skin were present 72 hours after application. Individual erythema scores of intact and abraded skin ranged from 1 to 3 with a mode of 2. Individual edema scores of intact and abraded skin ranged from 0 to 2 with a mode of 0 (ref, Appendix C).	CMP must be regarded as a primary skin irritant for man with a potential for causing skin destruction. Personnel should wear skin and eye protection and exercise extreme caution when handling this material.
0.5 ml technical grade CMP was applied to each of six rabbits.		
CMP in Hexane		
0.1 ml of technical grade CMP applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 1 to 2 with a mode of 1 after 24 hours. Individual edema scores ranged from 0 to 2 with a mode of 0.	Personnel coming into contact with technical grade compound should use eye and skin protection.
0.1 ml of 10 percent (w/v) of CMP in hexane applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 0 to 1 with a mode of 1 after 24 hours. Individual edema scores were all 0.	Personnel coming into contact with this compound at this concentration should use eye and skin protection.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
0.1 ml of 1 percent (w/v) solution of CMP in hexane applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 1 to 2 after 24 hours, with a mode of 2. Individual edema scores were all 0.	Personnel coming into contact with this compound at this concentration should use eye and skin protection.
0.1 ml of hexane applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 0 to 2 after 24 hours, with modes of 0 and 1. Individual edema scores ranged from 0 to 2 with a mode of 0 (ref, Appendix C).	Hexane by itself was slightly irritating to rabbit skin.
CMP in Acetone		
0.1 ml of technical grade CMP applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 1 to 2 after 24 hours, with a mode of 1. Individual edema scores ranged from 0 to 2 with a mode of 0.	Personnel coming into contact with technical grade compound should use eye and skin protection.
0.1 ml of 10 percent (w/v) solution of CMP in acetone applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 0 to 1 after 24 hours, with a mode of 0. Individual edema scores were all 0.	Compound at this concentration should not cause irritation to human skin, provided it is washed off immediately.
0.1 ml of 1 percent (w/v) solution of CMP in acetone applied to the clipped intact skin of five rabbits.	Individual erythema scores ranged from 0 to 1 after 24 hours, with a mode of 0. Individual edema scores were all 0.	Compound at this concentration should not cause irritation to human skin, provided it is washed off immediately.
0.1 ml of acetone applied to the clipped intact skin of five rabbits.	Individual erythema and edema scores were all 0 after 24 hours (ref, Appendix C).	Acetone by itself was not irritating to rabbit skin.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Photochemical Skin Irritation		
Studies		
Rabbits		
A single application (0.05 ml) of a 25 percent (w/v) solution of CMP in 95 percent (w/v) ethyl alcohol and a 5 percent (w/v) solution of oil of bergamot (positive control) in 95 percent ethyl alcohol where applied to the intact skin of six New Zealand White rabbits. After 5 minutes, the rabbits were exposed to ultraviolet (uv) light (365 nm) for 30 minutes from a distance of 10 to 15 cm. Following uv exposure of the rabbit, 0.05 ml of the test compound and positive control were applied to additional skin areas to serve as unirradiated control sites. Each area was graded for skin irritation reactions at 24, 48 and 72 hours after application using the grading scale in Appendix C.	CMP did not cause a photochemical irritation reaction under test conditions. However, an ethanol solution of CMP caused the same degree of erythema and edema at both irradiated and nonirradiated skin sites. Positive control application and irradiation caused greater irritant effects than in unirradiated areas.	Compound did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation reaction in humans. Ethanol solutions of the compound may cause a skin irritation reaction in humans.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Sensitization Studies		
Guinea Pigs (Male)		
Intradermal injection of 0.1 ml of suspension (w/v) of CMP or dinitrochlorobenzene (DNCB) in a mixture containing one volume of propylene glycol and 29 volumes of normal saline.		
Ten test guinea pigs receiving and challenged with a 0.1 percent suspension of CMP.	Challenge dose of test compound (last intradermal injection) at concentrations of 1.0 and 0.1 percent for CMP produced no greater response than did prior sensitizing doses.	Test compound did not sensitize guinea pigs and would not be expected to produce a sensitization reaction in humans.
Ten test guinea pigs receiving and challenged with a 0.01 percent suspension of CMP.	Positive control challenge produced sensitization in 10/10 guinea pigs.	
Ten test guinea pigs receiving and challenged with 0.1 percent suspension of DNCB.		
Ten cage control guinea pigs: five each receiving 0.1 percent suspension of compound without prior sensitizing doses; five receiving challenge doses of DNCB without prior sensitizing dose.	Challenge doses of CMP and DNCB in cage control guinea pigs produced no greater response than did initial injections of test animals.	

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Approximate Lethal Dose		
CMP		
Intraperitoneal		
Rat (male)	ALD-851 mg/kg. Lethargy and depressed activity noted in all doses above and including 567 mg/kg.	
Intravenous		
Rabbit (male) propylene glycol diluent	ALD-192 mg/kg. Lethal dosages were immediately accompanied by relaxation of muscular control.	
LD-50 Oral		
Rats (male)		
Six rats per dosage level technical grade material.	LD50-2243 mg/kg (1865-2697 mg/kg)* Death occurred at dosages of 1585 mg/kg and higher as well as signs of lethargy, ruffled coat and discharge from eyes.	CMP is classified as a moderately toxic compound. Parameters of classification are found in Appendix D.
Rats (female)		
Six rats per dosage level corn oil diluent	LD50-1650 mg/kg (1411-1928 mg/kg)* Death occurred at dosages of 1269 mg/kg and higher as well as signs of wet anal regions, red exudate around eyes and ruffled pelts. Lethal dosages produced lethagy and gasping.	
LD-50 Dermal		
Rabbits (male)		
Four rabbits per dosage level technical grade material.	LD_{50} - 6600 mg/kg (5516 to 7946 mg/kg).* Deaths occurred at 3000 mg/kg and above at 4 to 8 days after dosing as well as signs of decreased activity. Mild to severe primary skin irritation was noted at all dosage levels. No other signs were observed.	Compound causes skin damage and should be prevented from coming in contact with the skin. If skin is accidentally exposed, it should be flushed with copious amounts of water immediately. CMP is classified a slightly toxic compound. Parameters of classification are found in Appendix D.

* 95 percent confidence limits

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Acute Inhalation Vapor Exposures		
Single 8-Hour Saturated Vapor Exposures		
Rats		
Two groups of six male rats each were exposed to saturated vapors of CMP. Dispersion bubblers were held at 24° and 100°C, respectively. A control group of six male rats was exposed to chamber air only.	Nominal concentrations were: CMP (24°C)-0.02 mg/l CMP (100°C)-1.9 mg/l Animals from all groups showed no signs of toxicity during exposure and for 14 days thereafter. Body weight gain and organ to body weight ratios of exposed rats compared to control rats were not significantly different. No chemically induced histopathological lesions were observed in the heart, nasal turbinates, eye, stomach, small intestine, pancreas, large intestine, adrenal gland, bladder, muscle, bone, liver, lung, kidney, or testes of rats exposed to CMP vapors at 24° or 100°C.	CMP has a very low volatility and should present no hazard at room temperature due to the inhalation of vapors. Vapor exposure at 100°C for CMP over this period of time resulted experimentally in no deleterious effect.

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Test	Results	Interpretation
Acute Inhalation Aerosal Exposure		
Single 1-Hour Exposure		
Rats		
Two groups of 10 male rats each were exposed to aerosols of CMP. A Dautrebande D_{30} aerosol generator was used to disperse each compound at 24°C.	Exposure 1 Nominal concentration CMP-2.5 mg/l Exposure No. 2 Nominal concentration CMP-4.7 mg/l	Respiratory exposure to aerosols of this compound may cause respiratory distress and should be avoided.
A control group of 10 male rats was exposed to chamber air only.	Animals from all groups showed no signs of toxicity during exposure and for 14 days thereafter. Body weight gain and organ to body weight ratios of exposed rats compared to control rats were not significantly different.	Technical grade compound to be used with caution around the eyes and mucosa.
	No CMP exposure related histopathological lesions were observed in the nasal turbinates, trachea, liver, stomach, small and large intestine, pancreas, kidney, adrenal gland, testes, brain, skin, muscle or bone. Corneal damage was seen in five of the ten high exposure animals, 0 of 10 low exposure animals and 0 of 10 control animals. The scope of histologic changes consisted of edema, keratitis and pannus. Histologic changes related to the exposure were not observed in other structure of the eye. Pneumonitis was observed in the lungs of 2 of 10 high exposure animals, 5 of the 10 low exposure animals and 0 of 10 control animals.	If the compound should accidentally get into the eyes they should be flushed immediately with copious amounts of water.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Subchronic Inhalation		
Vapor Exposure		
Rats		
Two group of six male rats each were exposed to saturated vapors of CMP, 6 hours per day for 10 days. Dispersion bubblers were held at 24°C and 100°C, respectively. A control group of six male rats was exposed to chamber air only.	Nominal Chamber Concentrations were: CMP (24°C) - 0.02 mg/l CMP (100°C)- 1.74 mg/l Animals from all groups showed no signs of toxicity during exposure and for 14 days thereafter. Body weight gain and organ to body weight ratios of exposed rats compared to control rats were not significantly different. No chemically induced histopathological lesions were observed in the heart, nasal turbinates, eye, stomach, small intestine, pancreas, large intestine, adrenal gland, bladder, muscle, bone, liver, lung, kidney or testesof rats exposed to CMP vapors at 24° or 100°C.	CMP has a very low volatility and should present no hazard at room temperature due to the inhalation of vapors. Vapor exposure at 100° for CMP over this period of time resulted experimentally in no deleterious effects.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Prenatal Toxicity Studies		
Rats		
CMP, aspirin and corn oil were administered orally each to groups of 20 preimpregnated rats daily from day 6 through day 16 of gestation. Day 0 of gestation was counted as the day sperm was found in the vaginal smear. The females were sacrificed on day 20 of gestation by intracardic injection of sodium pentobarbital. The reproductive tracts were exposed by laparotomy and the corpora lutea, implantation sites and resorption sites were recorded. The fetuses were removed, examined for gross abnormalities, sex, weight and length. All grossly abnormal fetuses and 50 percent of the apparently normal fetuses were further studied as Bouin-fixed, freehand sections for soft tissue abnormalities or after alizarin red s staining for skeletal malformations. Dailey oral dosages were: 170 mg/kg CMP 330 mg/kg CMP 250 mg/kg Aspirin 2 ml/kg Corn Oil	Fetuses from CMP treated females showed no difference in fetal resorption or male/female sex ratios nor gross abnormalities of the fetus, fetal skeleton or soft tissue from solvent controls. Significantly lower average fetal weights and lengths were observed in the aspirin controls. Positive controls also showed a variety of abnormalities including flattened heads, craniorachioschisis, protruding tongue, anopthalmia, gastroschisis, hydrocephalus and missing coccygeal vertebrae. A significantly higher number of fetal resorptions were found in the aspirin controls when compared with solvent control and CMP groups. No other fetal abnormalities were observed in any fetus. No maternal deaths occurred during the test.	CMP administered to pregnant rats during gestation by intra-gastric intubation does not appear to present any significant hazard to the developing fetus.

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TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
In Vitro Mutagenic Evaluation*		
Microorganisms		
One strain of yeast, saccharomyces cerevisiae, strain D4 and five strains of Salmonella typhimurium (TA-1535, TA-4537, TA-1538, TA-98, TA-100) were used in evaluating the mutagenic potential of CMP. Liver tissue homogenates prepared from the livers of Sprague-Dawley adult male rats were used as the activators in the activation system, and no tissues were added to the nonactivated system. Positive and solvent controls were included. All plates were incubated for 48 to 72 hours at 37°C and scored for the number of colonies growing on each plate.	The results of the nonactivated and activated series were both negative.	This compound appeared to be nonmutagenic in the assays performed.

* Work contracted to Litton Bionetics, Kensington, Maryland (LBI Project No. 2547)

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
Enzyme Induction		
Rats-Sleeping Times		
Groups of male rats (10 per group) were pretreated for 4 consecutive days intraperitoneal with one of the following: Positive Control 100 mg/kg sodium phenobarbital Test Group 170 mg/kg CMP in corn oil Solvent Control 170 mg/kg corn oil Cage Control No prior injection On day 5 each group of rats received an intraperitoneal injection of hexobarbital (220 mg/kg). The sleeping times were started when a rat failed to right itself and continued until the rat was able to right itself twice.	The mean sleeping times for each of the groups are as follows: Sodium phenobarbital 23.71 min ± 6.30 CMP 87.17 min ±16.73 Corn Oil 67.10 min ±19.27 Cage Control 80.98 min ±17.80 CMP treated rats sleeping times were not statistically differcent from the solvent control or cage control as were the phenobarbital positive controls.	When tested as described, CMP was not found to be an inducer of hepatic microsomal enzyme activity.

6. DISCUSSION.

a. Animal data from skin irritation studies indicated that technical grade CMP should be handled with caution, using skin and eye protection equipment. If this compound comes into contact with unprotected skin or eyes it should be removed immediately.

b. CMP diluted with hexane was found to be more irritating to the skin of rabbits than equal concentrations using acetone as a diluent. Hexane alone was found to produce well defined erythema in rabbits 24 hours after application.

c. Single oral ingestion studies of CMP with male and female rats showed that little hazard would be expected from acute accidental ingestion.

d. CMP does not appear to present any significant hazard to subsequent generations, based on teratology studies and the results of mutagen testing on standard strains of bacteria and yeast.

e. The low degree of hazard from inhalation of the vapors of this compound was partly due to its low vapor pressure at room temperature. Increasing the ambient concentration to 1.39 mg/l by volatilizing the compound at 100°C also resulted experimentally in no deleterious effects.

f. Acute exposure of rats to aersols of CMP at nominal concentrations of 2.5 mg/l and 4.7 mg/l caused signs of lung irritation (pneumonitis). Rats exposed to the greater of the two concentrations exhibited corneal eye damage. Previous studies have demonstrated that the particles generated by the Dautrebande D_{30} aerosol generator are under 0.5 μ and that most of them are between 0.1 μ and 0.2 μ.[1] Particles of this size can penetrate and deposit in any area of the lung and then are likely to be the predominant particles involved in alveolor deposition and retention.[2] [3] These findings show that the major health hazard to be expected to man under these conditions would be eye and respiratory tract irritation.

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[1] Y. Alarie, "Irritating Properties of Airborne Materials to the Upper Respiratory Tract," Archives of Environmental Health, 13, 433-449 (1966)
[2] P. E. Morrow, "Evaluation of Inhalation Hazards Based Upon the Respirable Dust Concept and the Philosophy and Application of Selective Sampling," American Industrial Hygiene Association Journal, 25, 213-236 (1964)
[3] L. Dautribande, H. Beckmann, and W. Walkenhurst, "Studies on Deposition of Submicronic Dust Particles in the Respiratory Tract," A.M.A. Archives of Industrial Health, 19, 383-391 (1959)

g. At the present time, good industrial practices would indicate that mechanical control of vapors and aerosols of CMP in the working area would be necessary to contain and prevent possible exposure hazards to man. While environmental levels have not been established for airborne concentrations of CMP, the most likely processes requiring control are those in which fogs or mists are envolved.

7. CONCLUSION. Evaluation of toxicity data on rabbits, rats and guinea pigs indicates that technical grade CMP should present little acute toxic hazard to man, provided good industrial precautions relative to topically irritating material are employed.

8. RECOMMENDATIONS.

a. Personnel potentially exposed to the technical grade liquids of CMP must wear coveralls, and skin and eye protection devices.

b. Medical surveillance of workers involved with these compounds should take cognizance of the potential for irritation of the skin, eyes and respiratory tract.

c. Inhalation exposure to vapors and aerosols of CMP should be controlled by implementation of good industrial hygiene ventilation programs. Local exhaust ventilation may be required in operations where fogs and mists are envolved.

d. Personnel with respiratory disorders should avoid direct exposure to airborne concentrations of CMP.

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APPENDIX A

GLOSSARY OF RECURRING DEFINITIONS, ABBREVIATIONS AND SYMBOLS USED BY THE TOXICOLOGY DIVISION, USAEHA

Definitions of medical terms and abbreviations used in this report are in agreement with the New Gould Medical Dictionary, Second Edition, published by the Blakiston Division of McGraw-Hill Book Company, Inc. Statistical terms and abbreviations are in agreement with those found in J. Maxwell Little's, An Introduction to the Experimental Method, 1961, Burgess Publishing Company, Minneapolis, Minn. The following terms and abbreviations are either not found in the above references or have been modified to fit the special purposes of this report. Some of the terms have been included below for special emphasis.

WORD	DEFINITION
Acute Exposure	One exposure to exogenous test material for no longer than 8 hours. Animals are normally observed for 14 days after exposure.
Anophthalmia	Congenital absence of one or both eyes.
Approximate Lethal Dose	In range finding the first dose of the lowest series of three ascending doses (each being 50 percent higher in concentration than the previous) all of which produce fatalities.
Craniorachioschisis	Congenitally unclosed skull and spinal column.
Gastroschisis	Congenital defect in the abdomen wall, usually with protrusion of the viscera.
Hazard Evaluation	A study performed to estimate the degree of danger associated with the use of a material under specified conditions of use.
Hydrocephalus	A condition, usually congenital, marked by an excessive accumulation of fluid in the cerebral vertricles, dilating these cavities, thinning the brain, and causing a separation of the cranial bones.

WORD	DEFINITION
Nominal Concentration	Concentration of compound in the exposure chambers as determined by ascertaining the weight of the sample lost from the dispersion apparatus divided by total volume of chamber air used throughout the exposure time.
Primary Irritation	A local inflammatory reaction of the skin, produced by a compound, which does not produce destruction or irreversible change at the site of contact.
Subchronic Exposure	Repeated daily or constant exposure to a test material for no longer than 179 days or less than 2 days. Post observation period will vary.
Technical Grade Compound	As produced by the manufacturers of their commercial compound; definition dependent upon manufacturer's criteria.

ABBREVIATION	MEANING
ALD	approximate lethal dose
CMP	Carboranylmethyl propionate
LD_{50}	median lethal dose
>	is greater than
<	is less than

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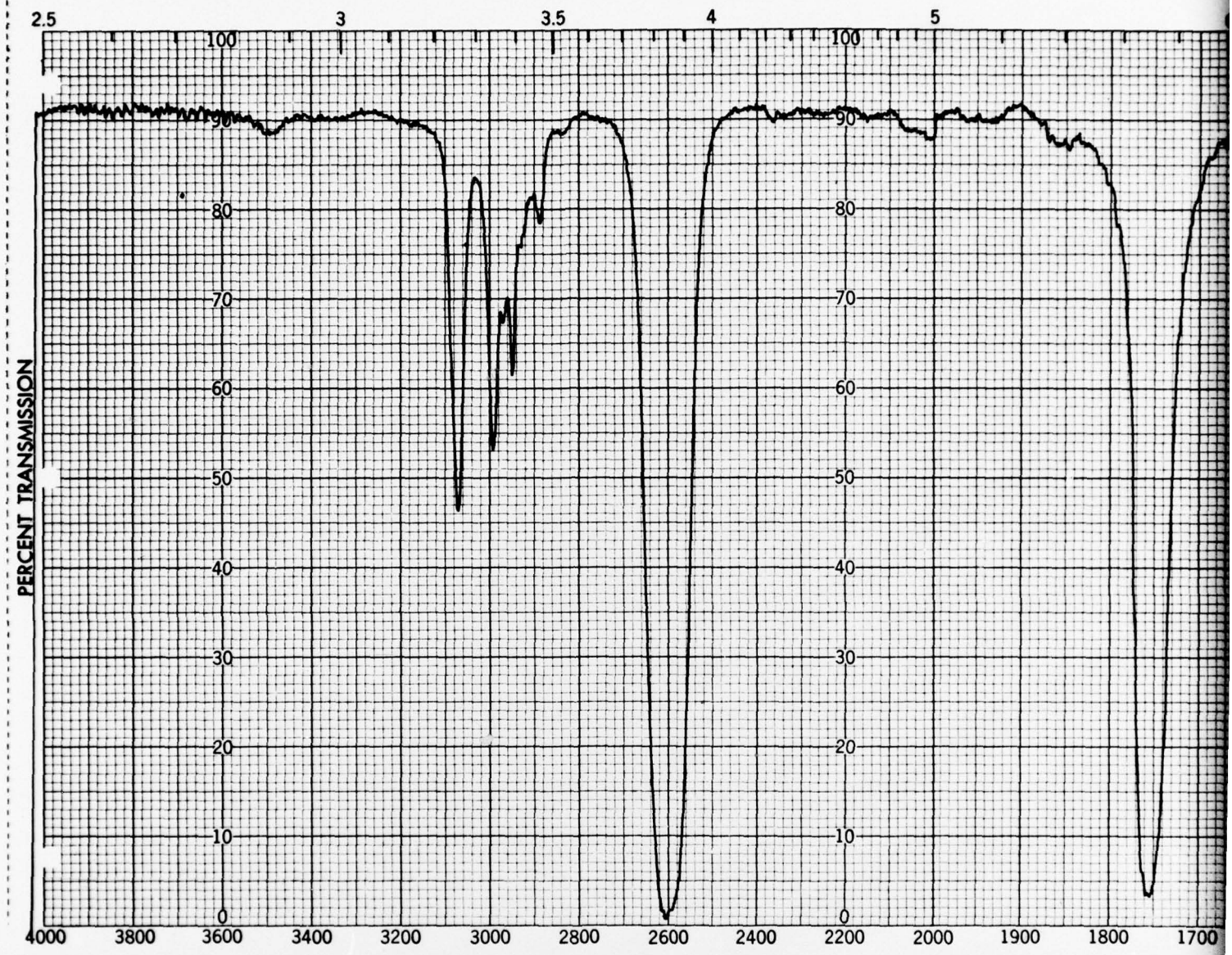
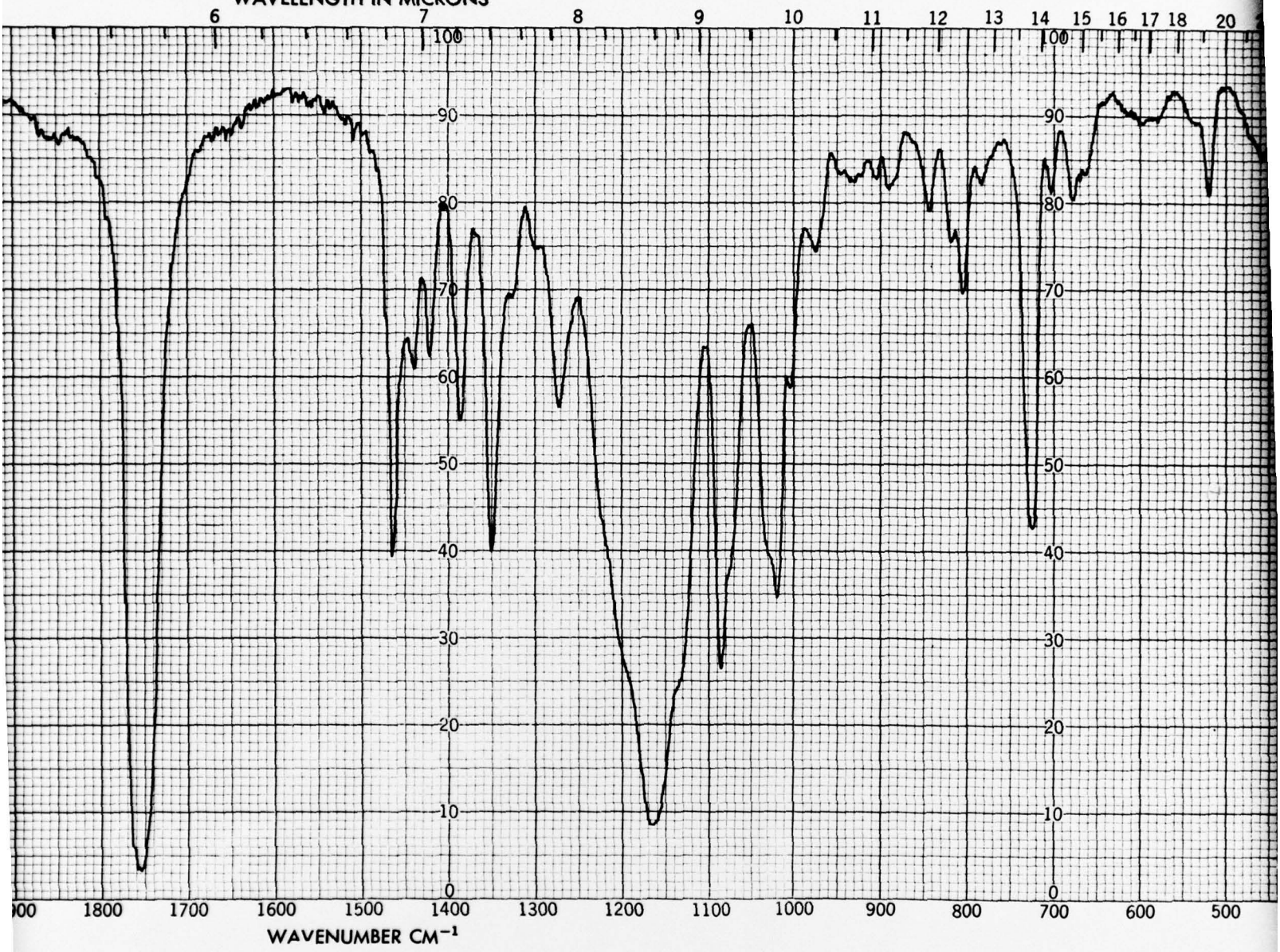


SAMPLE: CARBONYLMETHYL PROPIONA

SPEED: 200 CM $^{-1}$ /MIN

SLIT: ROUTINE

APPENDIX B



YLMETHYL PROPIONATE

GAIN: 3%

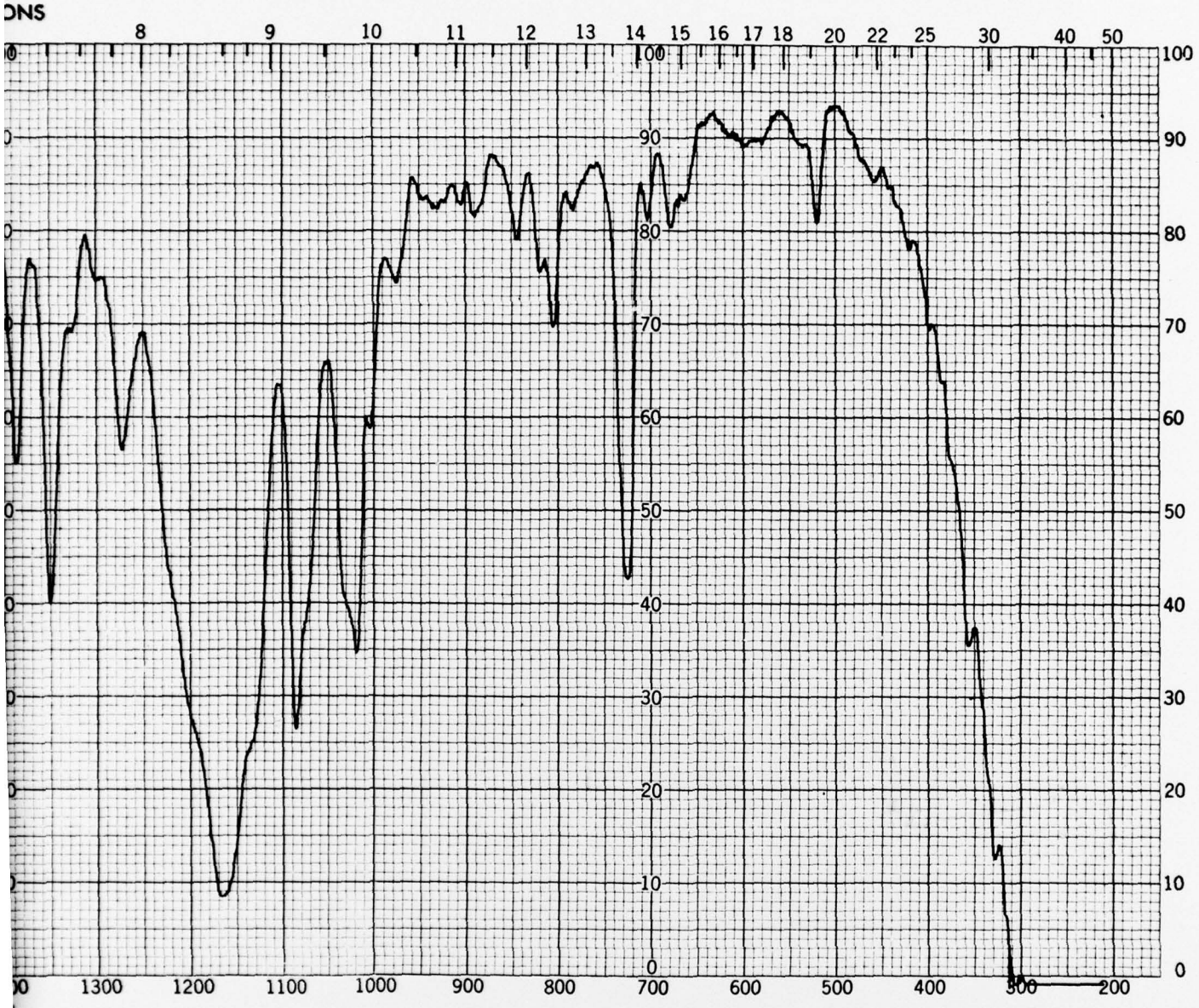
/MIN

PERIOD: 2

2

ORDINATE: 0-100%T

INFRARED SPECTRUM



AIN: 3%

RIOD: 2

DINATE: 0-100%T

3

APPENDIX C

EVALUATION OF SKIN REACTIONS*

Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness to slight eschar formation)	4

Edema Formation

No edema	0
Very slight (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

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* An individual irritation score is equal to the sum of the scores for edema formation and erythema and eschar formation.

APPENDIX D

TABULATION OF TOXICITY DOSES*

VARIOUS ROUTES OF ADMINISTRATION

Commonly Used Terms	LD_{50} Single Oral Dose Rats	Inhalation 4-Hr Vapor Exposure Mortality 2/6 - 4/6 Rats	LD_{50} Skin Rabbits
Highly toxic	50 mg/kg or less	100 ppm or less	43 mg/kg or less
Toxic	51-500 mg/kg	101-1,000 ppm	44-350 mg/kg
Moderatly toxic	501-5,000 mg/kg	1,001-10,000 ppm	351-2,800 mg/kg
Slightly toxic	5,001-15,000 mg/kg	10,001-100,000 ppm	2,801-22,600 mg/kg
Practically nontoxic	above 15,000 mg/kg	>100,000 ppm	above 22,600 mg/kg

* Adapted from Hodge, H. C. and Sterner, J. H. American Industrial Hygiene Association Quarterly, 10:4.93 (December 1943)